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REMARKS

Claim 1-12, 14, 18, 20, 21, 23, 26, 28-32 and 35-47 are pending. No new matter has been added by way of the present amendment. For instance, claims 19, 27, 33 and 44 have been cancelled. Claims 1 and 2 have been amended to remove the functional language relating to "fluorescence". Claim 18 has been amended to specifically define the amino acid substitution and to specifically define the location of the chromophore. The amendments to claim 18 are supported by, for instance, canceled claim 27, original claim 6, and page 3, lines 10-20 of the present specification. Claims 14 and 23 have been amended to remove the "functional GFP analog" language. Claims 28-32 have been amended to depend upon claim 2. New claim 35 is supported by claim 18 as well as the present specification at page 3, lines 10-20. New claims 36, 37 and 46 are supported by the present specification at page 2, lines 7-13 and page 7, lines 23-24. New claims 37, 38, 39, 41 and 42 are supported by claims 28, 29, 30, 31 and 32, respectively. New claims 43-45 are supported by the present specification at page 3, lines 5-9. Lastly, new claim 47 is supported by originally filed claim 14. Accordingly, no new matter has been added.

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In view of the following remarks Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Objections to the Claims

The Examiner has objected to claims 33 and 34 under 37 C.F.R. §1.75 asserting that they are substantial duplicates of claims 20 and 21, respectively. Applicants respectfully traverse this objection and submit that claims 33 and 34 have been canceled. Thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Objection to the Specification

At pages 2 and 3 of the outstanding Office Action the Examiner has objected to the specification for allegedly failing to comply with the sequence rules and regulations. In particular, the Examiner notes that the specification refers to F64L-Y66-GFP, F64L-GFP, F64L-S65T-GFP and GFP which are SEQ ID NO: 16, 18, 20 and 22 respectively. Applicants have amended the first recitation of these sequences in the "Summary of the Invention" to refer to the correct SEQ ID NOS. Accordingly, this objection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues Under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 1-12, 14, 18-21, 23 and 26-34 under 35 U.S.C. §112, second paragraph for the reasons recited at pages 3 and 4 of the outstanding Office Action. Applicants respectfully traverse each of these rejections.

First, the Examiner asserts that the recitation of the limitation "increased fluorescence... relative to" in claims 1, 2 and 18 is unclear. Applicants traverse and submit that this language has been canceled from claims 1 and 2. Moreover, claim 18 has been amended to indicate that the increased fluorescence is at the same wavelength. Accordingly, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Second, the Examiner has rejected claims 18 and 19 for the recitation of "position 1" asserting that such position with respect to the "chromophore" is unknown. The Examiner further asserts that the "chromophore" is not properly defined. Applicants respectfully traverse this rejection. Applicants submit that claim 19 has been canceled and claim 18 has been amended to correct this issue. Thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Third, the Examiner asserts that the recitation of "functional GFP analog" in claim 14 lacks antecedent basis in claim 1. Applicants respectfully traverse and submit that this language has been deleted from claim 14. Thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Fourth, the Examiner asserts that the limitations of claims 1 and 18 as well as claims 14 and 23 are unclear due to the recitation of a "functional analog" of GFP. Applicants traverse and submit that this language has been removed from these claims. Thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues Under 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 14, 18-21, 23, 33 and 34 under 35 U.S C. §112, first paragraph for the reasons recited at pages 4-6 of the outstanding Office Action. Applicants traverse.

The Examiner asserts that language relating to the "functional analog" of GFP in each of claims 14, 18-23 and 26-34 is not adequately described in the present specification. Applicants traverse; however, in an effort to further prosecution applicants have amended the relevant claims to

remove the recitation of the "functional analog" language. Thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Issues Under 35 U.S.C. §102(e)

The Examiner has rejected claims 14, 18, 20, 21, 23, 33 and 34 under 35 U.S.C. §102(e) as being anticipated by Chalfie et al., USP 5,491,084. Applicants respectfully traverse this rejection. Each of the claims rejected by the Examiner requires a nucleic acid molecule that encodes a GFP that is modified by an amino acid substitution at the phenylalanine residue immediately upstream up the chromophore. In particular, the phenylalanine is substituted with an amino acid selected from the group consisting of Leu, Ile, Val, Gly, and Ala. The Chalfie reference fails to suggest or disclose such a nucleic acid. Thus, there is no anticipation based upon Chalfie. Reconsideration and withdrawal of this rejection are respectfully requested.

The Examiner has also rejected claim 14 under 35 U.S.C. §102(e) as being anticipated by Tsein et al., USP 5,625,048. Applicants respectfully traverse this rejection. Similar to that argued above with respect to the Chalfie reference, Tsein fails to suggest or disclose the currently claimed nucleic acid

molecule. That is, Tsein fails to suggest or disclose a nucleic acid molecule that encodes a GFP that is modified by an amino acid substitution at the phenylalanine residue immediately upstream up the chromophore. Thus, this rejection is moot. Reconsideration and withdrawal thereof are respectfully requested.

Obviousness-Type Double Patenting

The Examiner has provisionally rejected claims 1-3, 8, 9, 10, 11, 12, 13-21, 26-29, 33 and 34 under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 10-15 of copending application number 09/619,310. Applicants respectfully traverse this rejection. Applicants note that the scope of the claims has not being decided in either the present application or copending application serial number 09/619,310. As such, Applicants draw the Examiner's attention to MPEP §804 I-B wherein it is explained that if the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the Examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection, which has presumably been presented

in the other application, into an actual double patenting rejection at the time the first application issues as a patent.

Initialed Form PTO-1449

On March 6, 2003, Applicants filed an Information Disclosure Statement which included references of record in parent application serial number 09/619,310. The Examiner is respectfully requested to provide an intialed copy of the Form PTO-1449 indicating these references have been considered and will be listed on the front of any subsequently issuing United States Patent.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Registration No. 42,874 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

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required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

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LRS/CAM/gh
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Attachments: Version with Markings to Show Changes Made

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification was amended as follows:

The paragraph starting at page 2, line 31 and ending at page 3, line 4 was amended as follows:

The purpose of the present invention is to provide novel fluorescent proteins, such as F64L-GFP (SEQ ID NO: 18, hereinafter referred to as F64L-GFP), F64L-Y66H-GFP (SEQ ID NO: 16, hereinafter referred to as F64L-Y66H-GFP) and F64L-S65T-GFP (SEQ ID NO: 20, hereinafter referred to as F64L-S65T-GFP) that result in a cellular fluorescence far exceeding the cellular fluorescence from cells expressing the parent proteins, i.e. GFP (SEQ ID NO: 22, hereinafter referred to as GFP), the blue variant Y66H-GFP and the S65T-GFP variant, respectively. This greatly improves the usefulness of fluorescent proteins in studying cellular functions in living cells.

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IN THE CLAIMS:

Claims 19, 27, 33 and 34 were cancelled.

The claims were amended as follows:

1. (Amended) A nucleic acid molecule comprising a nucleotide sequence encoding a Green Fluorescent Protein (GFP) polypeptide that has the amino acid sequence of SEQ ID NO:22 with the exception that a Leu residue is substituted for the Phe residue at position 64 of SEQ ID NO:22[, wherein said substituted GFP exhibits increased fluorescence at a temperature of 30°C or above, relative to the GFP that has the amino acid sequence of SEQ ID NO:22, when expressed in a host cell].

2. (Amended) A nucleic acid molecule comprising a nucleotide sequence encoding a Green Fluorescent Protein (GFP) polypeptide that has the amino acid sequence of SEQ ID NO:22 with the exception that an amino acid residue selected from the group consisting of Leu, Ile, Val, Gly and Ala is substituted for the Phe residue at position 64 of SEQ ID NO:22[, wherein said substituted GFP exhibits increased fluorescence at a temperature of 30°C or above, relative to the GFP that has the amino acid sequence of SEQ ID NO:22, when expressed in a host cell].

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14. (Twice Amended) A nucleic acid molecule comprising a nucleotide sequence encoding a protein of interest fused to a nucleotide sequence encoding a Green Fluorescent Protein (GFP) [or a functional GFP analogue] according to claim 1.

18. (Amended) A nucleic acid molecule comprising a nucleotide sequence encoding a Green Fluorescent Protein (GFP) [or a functional GFP analogue] having an amino acid sequence [which is modified by amino acid substitution compared with the amino acid sequence of SEQ ID NO:22, by at least an amino acid substitution at position 1 preceding] in which the amino acid Phe immediately upstream of the chromophore is substituted with at least an amino acid selected from the group consisting of Leu, Ile, Val, Gly, and Ala, wherein said chromophore has an amino acid sequence selected from the group consisting of SerTyrGly, SerHisGly, ThrHisGly and ThrTyrGly, and wherein said substituted GFP exhibits increased fluorescence at the same wavelength at a temperature of 30°C or above, relative to the GFP lacking the above substitution [that has the amino acid sequence of SEQ ID NO:22], when expressed in a host cell.

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23. (Twice Amended) A nucleic acid molecule comprising a nucleotide sequence encoding a protein of interest fused to a nucleotide sequence encoding a Green Fluorescent Protein (GFP) [or a functional GFP analogue] according to claim 18.

Claims 25-47 were added.